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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,825	10/01/2001	Nicole Dusch	213545US0X	3991

22850 7590 12/04/2003

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/965,825	DUSCH ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *2-4,13 and 19-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-12, 14-18 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3/6/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-31 are pending.

Applicant's amendment of claims 14, 22 and addition of claim 31 in a communication filed on 9/12/2003, is acknowledged.

Applicant's election with traverse of Group V, claims 1, 6-12 drawn to a process for preparing D-pantothenic acid using a coryneform bacteria which has an attenuated poxB gene, wherein said gene is that of SEQ ID NO: 1, in a communication filed on 9/12/2003, is acknowledged.

Applicant's traverse is on the ground(s) that statements made in the restriction requirement of Paper No. 7, mailed on 8/12/2003, indicating why restriction is proper in regard to product and processes of use are merely conclusory and unsupported by further examples or reasoning. Applicants further submit that even if the allegations made by the Office are correct, there is no evidence of record showing that the proposed alternative uses are materially different from the claimed processes. In addition, Applicants argue that the Office has not shown how Groups I-V, VII, IX, VI, Groups II-V, VII, IX, and VIII, and Groups I-V, VII, IX are unrelated nor has the Office indicated how Groups VI, VIII, and X-XII are unrelated. Applicants submit that the search of all the claims would not impose an undue burden on the Office.

Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement. As clearly indicated in Paper No. 7, the polynucleotides of Inventions X-XII can be used in the methods of Inventions I-III as well as to recombinantly produce the corresponding polypeptides. In addition, it was indicated in Paper No. 7 that the polynucleotides of Inventions X-XI can be used in the method of Invention IX as well in the recombinant production of the corresponding polypeptides. Furthermore, the polynucleotides of Inventions X-XII can be used as probes. In regard to the bacteria of Invention VIII, it was clearly stated in Paper No. 7 that such bacteria can be used in the

method of Invention I as well as to produce other proteins which are specific to such bacteria. Therefore, the Examiner has provided clear examples and reasoning as to why the inventions are distinct according to MPEP 806.05(h). In regard to Applicant's arguments that there is no evidence of record showing the proposed alternative uses, it is noted that it is well known in the art that genes encode proteins and that polynucleotides encoding proteins can be used to recombinantly produce such proteins in host cells. Furthermore, the claims clearly state that the polynucleotides of SEQ ID NO: 6, 7 and 12 are genes, i.e. "wherein said gene is that of SEQ ID NO: #". As such, the alternative use cited for the polynucleotides of SEQ ID NO: 6, 7 and 12 is well known. In regard to alternative uses for the bacteria of Invention VIII, it is well known in the art that all organisms, such as bacteria, make their own proteins. Therefore, the bacterium of Invention VIII can be used to make the recombinant protein encoded by the polynucleotide of SEQ ID NO: 12 as well as its own proteins.

In regard to arguments that the Office in the cases where the inventions were deemed unrelated did not provide a statement as to how they are unrelated, it is noted that, as shown in Paper No. 7, in each case the Examiner provided a statement as to why they were deemed unrelated. As stated in Paper No. 7, the microorganism of Invention VI is neither used nor made by the processes of Inventions I-V, VII or IX. This is evidenced by the claims themselves in Inventions I-V, VII and IX which do not recite the microorganism of Invention VI. However, even if they were related as product (microorganism) and process of use, they would be deemed distinct for the same reasons provided in regard to the bacteria of Invention VIII and the process of Invention I. Similarly, the microorganism of Invention VIII is neither used nor made by the processes of Inventions II-V, VII or IX as evidenced by the method claims themselves which do not recite the microorganism of Invention VIII. In regard to Inventions VI, VIII, X-XII, the Examiner clearly stated in Paper No. 7 that each of these inventions comprise a chemically unrelated structure and indicated why these are chemically unrelated structures. See paragraph 9 in page 5. As such, it is unclear as to how the Office has failed to show how these inventions are unrelated. In

regard to arguments that examination of all the inventions would not impose a serious burden on the Office, it is noted that a comprehensive search would require a sequence, patented and non-patented literature, as well as class/subclass searches for each of the claimed inventions. As such, a search of all the invention would impose an undue burden on the Office.

As a result of a sequence search of SEQ ID NO: 1, it was found that SEQ ID NO: 3 is a fragment of SEQ ID NO: 1 and SEQ ID NO: 4 comprises SEQ ID NO: 1. As such, elected Group V as well as Group IV and VII will be rejoined for examination on the merits. Newly added claim 31 is directed to the elected invention and will be examined.

The requirement in regard to the remaining groups is deemed proper and therefore is made FINAL.

Claims 1, 5-12, 14-18 and 31 are being examined. Claims 2-4, 13, 19-30 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

1. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to GERMANY 100 48 604.5 filed on 09/30/2000, and GERMANY 101 17 085.8 filed on 04/06/2001. It is noted, however, that applicant has not filed a certified copy of the applications as required by 35 U.S.C. 119(b).

2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Germany DE10047142.0 on 9/23/2000. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter (10/1/2001).

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 3/6/2002 is acknowledged. The reference labeled as AW has not been considered since it lacks a publication date. The remainder of the submission is in compliance with the provisions of 37 CFR 1.97 and is being considered by the examiner.

4. A list of applicant's pending applications which may be related to the present application, submitted on 10/18/2002, is acknowledged.

5. A list of applicant's pending applications which may be related to the present application, submitted on 6/17/2003, is acknowledged.

Claim Objections

6. Claims 1 and 14 are objected to because of the following informalities: the terms "pantothenoic" and "pantothnic" should be "pantothenic". Appropriate correction is required.

7. Claims 11 and 17 are objected to because of the following informalities: the term "acteoglutamicum" should be "acetoglutamicum" and the term "coryneformbacterium" should be "corynebacterium". Appropriate correction is required.

8. Claims 1, 5, 8, 9, 12, 14, 15, 18, 31 are objected to due to the recitation of "poxB", "panB", "panC", "panD", and "ilvD". While these terms are related to gene nomenclature, these terms should not be recited in the claims without at least once reciting the protein being encoded by these genes. For examination purposes, it will be assumed that the term "poxB" refers to a gene encoding pyruvate oxidase, the term "panB" refers to a gene encoding ketopantoate hydroxymethyl transferase, the term "panC" refers to a gene encoding pantothenate synthetase, the term "ilvD" refers to a gene encoding dihydroxy-acid dehydratase and the term "panD" refers to a gene encoding aspartate 1-decarboxylase. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1, 5-8, 10-12, 14-18 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 1 (claims 5-8, 10-12 and 31 dependent thereon) is indefinite in the recitation of "attenuated poxB gene" for the following reasons. While the term "attenuation" has been defined in the specification as "reduction or elimination of the intracellular activity of one or more enzymes (proteins) in a microorganism", this definition refers to an enzyme (protein) but not to a gene (polynucleotide). As such, it is unclear if the term "attenuated poxB gene" refers to any modification in the gene which would result in the pyruvate oxidase encoded by such gene to have reduced or no activity, or if it refers to changes to the gene which may not affect the activity of the pyruvate oxidase encoded by such gene. For examination purposes, it will be assumed that the term refers to any modification in the gene which would result in the pyruvate oxidase encoded by such gene to have reduced or no intracellular activity. Correction is required.

12. Claim 14 (claims 15-18 dependent thereon) is indefinite in the recitation of "attenuated poxB expression" for the following reasons. As indicated above, the term "attenuation" has been defined in regard to enzymes and not genes. Therefore, it is unclear if the term refers to a reduction in transcription of the gene. Furthermore, even if the term is interpreted as "reduced transcription of the poxB gene", the term is unclear since according to the specification, transformation of the coryneform bacteria with the vector comprising the polynucleotide of SEQ ID NO: 3 would result in homologous recombination with the poxB gene already present in that coryneform bacteria, which in turn will result in a truncated poxB gene which no longer encodes a fully active pyruvate oxidase. Therefore, it is unclear as to how one can

select for bacteria having low transcription of the poxB gene if the homologous recombination does not result in changes related to transcription. For examination purposes, it will be assumed that the term's intended meaning is "low or no pyruvate oxidase activity". Correction is required.

13. Claims 8 and 15 are indefinite in the recitation of "nucleotide sequence which hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NO: 1.." for the following reasons. As known in the art, hybridization occurs among molecules. Sequence are graphical representations of the order in which nucleotides/amino acids are arranged in a molecule. Therefore, it is unclear as to how a sequence can hybridize to another sequence. For examination purposes, it will be assumed that the intended meaning of the term is "polynucleotide which hybridizes under stringent conditions to the polynucleotide of SEQ ID NO: 1..". Correction is required.

14. Claims 8 and 15 are indefinite in the recitation of "PoxB protein" and "PoxB activity". While the poxB gene encodes a pyruvate oxidase, it is unclear if a PoxB protein is different from a pyruvate oxidase. Furthermore, it is unclear if PoxB activity is any different from pyruvate oxidase activity. For examination purposes, it will be assumed that PoxB protein is equivalent to pyruvate oxidase and PoxB activity is equivalent to pyruvate oxidase activity. Correction is required.

15. Claim 15 is indefinite in the recitation of "wherein said poxB gene" since there is no antecedent basis for the gene. For examination purposes, the term will be interpreted as "wherein the coryneform bacteria having low or no pyruvate oxides activity contains a poxB gene which hybridizes under.....". Correction is required.

16. Claims 18 and 31 are indefinite in the recitation of "gene whose expression is enhanced" for the following reasons. While the term "enhancement" has been defined in the specification as "the increase in the intracellular activity of one or more enzymes in a microorganism", this definition refers to enzymes (proteins) and not to genes (polynucleotides). As such, it is unclear if the term "gene whose expression is enhanced" refers to any modification in the gene such that the intracellular activity of the corresponding

enzyme is increased, or if it is limited to an increase in transcription of the gene, i.e. more mRNAs made. For examination purposes, the term will be interpreted as "gene modified in any way such that the intracellular activity of the corresponding enzyme is increased". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1, 5-12, 18 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 6-7, 10 and 11 are directed to a process for preparing D-pantothenic acid by culturing a genus of coryneform bacteria comprising a genus of genes encoding pyruvate oxidase wherein said genes have been modified in any way such that the pyruvate oxidase encoded by such genes have reduced or no intracellular activity. See claim interpretation above. Claims 5 and 8 are directed to the process of claim 1 as indicated above with the added limitation that the gene encoding pyruvate oxidase (1) comprises SEQ ID NO: 4 or (2) hybridizes under stringent conditions to the polynucleotide of SEQ ID NO: 1. Claim 9 is directed to the process of claim 1 wherein the genes encoding pyruvate oxidase in said genus of coryneform bacteria are eliminated. Claims 12 and 31 are directed to the process of claim 1 as indicated above with the added limitation that the coryneform bacteria further comprises a genus of genes encoding ketopantoate hydroxymethyl transferases, pantothenate synthetases, dihydroxy-acid dehydratases and/or aspartate 1-decarboxylases, wherein these genes are modified in any way such that the intracellular activity of the corresponding enzymes is increased.

While the specification discloses the C. glutamicum poxB gene and a method to produce D-pantothenic acid in C. glutamicum by inactivating the C. glutamicum poxB gene wherein said inactivation occurs by transforming a C. glutamicum bacterium with a vector comprising a fragment of the C. glutamicum poxB gene such that homologous recombination would occur and a deletion to the poxB gene results, and the specification also discloses where one can obtain the structures of the C. glutamicum panB, panC, panD, and ilvD genes, the specification is silent in regard to (1) the structures of other genes from other organisms encoding pyruvate oxidases including the structures of any coryneform bacteria poxB gene, (2) other modifications to the genes of (1), the gene of SEQ ID NO: 4, or structural homologs of the polynucleotide of SEQ ID NO: 1 that hybridize under stringent conditions, which would result in the corresponding pyruvate oxidases to have reduced or no intracellular activity, such as mutations (i.e. insertions, deletions or substitutions) either in the regulatory region of such genes which would reduce the transcription of the genes or mutations in the coding region which would result in pyruvate oxidases with little or no activity, (3) the structures of other genes from other organisms, including other coryneform bacteria, encoding ketopantoate hydroxymethyl transferases, pantothenate synthetases, dihydroxy-acid dehydratases and aspartate 1-decarboxylases, or (4) other modifications to the genes of (3) which would result in the intracellular activity of the corresponding enzymes to increase, such as mutations either in the regulatory region of such genes to increase transcription, or mutations in the coding region which would result in higher enzymatic activity.

The argument can be made that the structures of the recited genes, as required by the method claimed, can be isolated/made by structural homology using the structures disclosed by the specification or those of the prior art. However, the state of the art teaches that a high degree of structural homology may not result in functional homology. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-

6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. In addition, while increasing the intracellular activity of an enzyme can be achieved by increasing transcription using a strong promoter and decreasing the intracellular activity of an enzyme can be achieved by deleting a major portion of a gene, the claims as indicated above encompass any modification to the genes which would result in an increase or decrease in the activity of the corresponding enzymes. The specification discloses a few species of the genera of genes encompassed by the claims required by the method claimed, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of the claimed method. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

19. Claims 1, 5-12, 18 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a process for the production of D-pantothenic acid in C. glutamicum by inactivating the C. glutamicum poxB gene wherein said inactivation occurs by transforming a C. glutamicum bacterium with a vector comprising a fragment of the C. glutamicum poxB gene such that homologous recombination would occur and a deletion to the poxB gene results, and (2) a process as described above wherein at least one of the C. glutamicum panB, C. glutamicum panC, C. glutamicum panD, or C. glutamicum ilvD genes are over expressed by using a strong promoter, does not reasonably provide enablement for (1) a process for the production of D-pantothenic acid wherein said

process comprises culturing any coryneform bacteria containing any gene encoding a pyruvate oxidase, wherein said gene has been modified in any way such that the corresponding pyruvate oxidase has reduced or no intracellular activity, (2) a process for the production of D-pantothenic acid wherein said process comprises culturing any coryneform bacteria containing the gene of SEQ ID NO: 4 or a gene which hybridizes to the polynucleotide of SEQ ID NO: 1, wherein said genes have been modified in any way such that the corresponding pyruvate oxidases have reduced or no intracellular activity, or (3) a process for the production of D-pantothenic acid wherein the process comprises culturing any coryneform bacteria which has its poxB gene deleted.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims, as described above, is not commensurate with the enablement provided by the disclosure with regard to the unknown gene structures and unknown gene modifications required to practice the claimed method. As indicated above, the specification discloses the C. glutamicum poxB gene and a method to produce D-pantothenic acid in C. glutamicum by inactivating the C. glutamicum poxB gene wherein said inactivation occurs by transforming a C. glutamicum bacterium with a vector comprising a fragment of the C. glutamicum poxB gene such that homologous recombination would occur and a deletion to the poxB gene results. The specification also discloses where one can obtain the structures of the C. glutamicum panB, panC, panD, and ilvD genes. However the specification fails to disclose (1) the structures of other genes from other organisms, including other coryneform bacteria, encoding pyruvate oxidases, ketopantoate hydroxymethyl transferases, pantothenate synthetases, dihydroxy-acid dehydratases and aspartate 1-decarboxylases, and (2) other modifications to the recited

genes, including the gene of SEQ ID NO: 4 and structural homologs of the polynucleotide of SEQ ID NO: 1 that hybridize under stringent conditions, which would result in the corresponding enzymes to have reduced/increased intracellular activity, such as mutations (i.e. insertions, deletions or substitutions) either in the regulatory region of such genes which would reduce/increase the transcription of the genes or mutations in the coding region which would result in reduced/increased activity for the corresponding enzymes.

The state of the art teaches the unpredictability of determining function using structural homology and discloses examples of how small structural changes can lead to major changes in function. See the teachings of Broun et al., Van de Loo et al., Seffernick et al., and Witkowski et al. already discussed. As such, one of skill in the art would require some knowledge or guidance as to the structure of all the genes encompassed by the claims. In addition, since the claims encompass modifications to the coding regions of the genes such that the corresponding enzymes have increased or reduced activity, one of skill in the art would require some knowledge as to which are the critical structural elements in those enzymes which correlate with activity as well as which amino acids can be substituted, deleted or inserted such that the activity of such enzymes can be increased or decreased. Furthermore, as indicated above, no disclosure has been provided in regard to which modifications can be made in the regulatory elements of the recited genes which would result in increase/decrease transcription of the genes. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge as to the structures of the genes recited, the lack of knowledge about the critical structural elements associated with the desired enzymatic activity, the lack of knowledge about which amino acids in the enzymes recited can be modified to increase or reduce activity, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those genes recited in the claim, determine which modifications to the regulatory elements of such genes would result in increased/decreased transcription,

and which modifications in the coding regions of such genes would result in the corresponding enzyme to have increased/reduced activity. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Conclusion

20. No claim is in condition for allowance.

21. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
November 21, 2003

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600